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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,655	01/07/2002	Andrew Darrow	ORT-1566	3674

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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1652	3

DATE MAILED: 07/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,655	DARROW ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Preliminary Amendment

Applicant's Preliminary Amendment A, Paper No. 2 filed January 7, 2002, has been entered, canceling claims 1-24 and 27 and providing a reference at line 1, page 1, of the specification to the parent application serial No. 09/386,653, which issued on October 1, 2002, as U.S. Patent No. 6,458,564, made of record herewith.

Claim Rejections - 35 USC §112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25 and 26 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 10, to which claims 25 and 26 refer, was canceled with Paper No. 2, thus claims 25 and 26 are construed herein according to the definition of a "protein . . . that functions as protease T protein" provided in the paragraph spanning pages 6-7 of the specification, which embraces divergent proteases having activity substantially similar to that of the native human serine protease T having the amino acid sequence set forth in SEQ ID NO:7. The specification provides an adequate written description of only one "functional derivative" of the native protease T amino acid sequence set forth in SEQ ID NO:7 which is the zymogen fusion having the amino acid sequence set forth in SEQ ID NO:9. There is no evidence in the specification that Applicant possessed any other derivative, or a fragmentary, amino acid sequence differing from the amino acid sequences of SEQ IDs NOs:7 and 9 at the time the parent application was filed, thus Applicant could not have possessed a non-pharmaceutical composition comprising such alternative proteins at the time the parent application was filed. While Applicant and others can replace, e.g.,

the native signal peptide of the disclosed human serine protease T with a different signal peptide region just as Applicant introduced an alternative signal peptide, or add a polyhistidine tag to the amino acid sequence, or provide an alternative propeptide region such as Applicant had in preparing a baculovirus vector expression construct, nothing in the specification shows that Applicant had determined, or even contemplated, those positions among the carboxyl-proximal 260 amino acids of the human serine protease T that might be altered, nor the nature of any amino acid substitution save for those made in preparing the zymogen fusion of SEQ ID NO:9, nor any deletion of amino acids, to generate alternative fragments or proteases. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification provides no written description supporting the subject matters of non-pharmaceutical compositions comprising such proteases of claims 25 and 26, which are considered to be entirely prospective where there is no description of their "relevant identifying characteristic[s]" such that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Claims 25 and 26 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for non-pharmaceutical compositions comprising a human serine protease T having the catalytic domain amino acid sequence set forth in SEQ ID NO:7, does not reasonably provide enablement for non-pharmaceutical compositions comprising proteases having amino acid sequences that diverge from the catalytic domain of the protease comprised by SEQ ID NO:7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 10, to which claims 25 and 26 refer, was canceled with Paper No. 2. Thus claims 25 and 26 are construed according to the definition of a "protein . . . that

functions as protease T protein" provided in the paragraph spanning pages 6-7 of the specification. It is agreed that the state of the art taken together with the specification enables the preparation of serine proteases that retain the amino acid sequence of the catalytic domain present both in the native protease T having the amino acid sequence set forth in SEQ ID NO:7 and in the zymogen-protease T fusion protein having the amino acid sequence set forth in SEQ NO:9, but having a signal peptide domain and propeptide domain replaced by similar domains of other serine proteases. Claims 25 and 26 describe non-pharmaceutical compositions that embrace divergent proteases wherein catalytic domains may have arbitrary assignments of any or all amino acid deletions, additions, or substitutions in the amino acid sequence of the human protease T catalytic domain of SEQ ID NO:7, beyond the few amino acid substitutions disclosed at the amino-proximal border of the catalytic domain of the zymogen-protease T fusion protein having the amino acid sequence set forth in SEQ ID NO:9. Yet the specification does not teach one of skill in the art where, or how, nucleic acid sequences encoding the T protease catalytic domain comprised by SEQ ID NO:7 might be altered by introducing undisclosed modifications yet permit expression of a functioning protease catalytic domain having unspecified amino acid insertions, deletions, or substitutions anywhere, in any combination or pattern.

It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of enablement). The standard set by the CCPA, the predecessor of the Court of Appeals for

the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope of guidance provided by the specification and the scope asserted in the claimed subject matter. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); see also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The standard set by the CCPA was approved by the Federal Circuit in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). Applying the "*Forman*" factors discussed in *Wands*, to the scope of the claims rejected, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequences of the catalytic domain of the T protease comprised by SEQ IDs NOs:7 and 9,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no catalytic domains of related serine proteases have sustained alterations beyond that disclosed in the fusion protein having the amino acid of SEQ ID NO:9 yet retained their proteolytic activity.

The scope of the claimed subject matter embracing nucleic acid sequences encoding proteins having undisclosed amino acid sequences differing from the protease T catalytic domain amino acid sequences within SEQ IDs NOs:7 and 9 embraced by the definition at pages 6-7 of the specification with which claim 25's limitation, "protein of claim 10", must be construed.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25 and 26 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. Claims 25 and 26 are indefinite in their dependency from the cancelled claim 10, thus rewriting claim 25 in independent form will overcome this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(e), (f) or (g) prior art under 35 U.S.C. §103(a).

Claims 25 and 26 are rejected under 35 U.S.C. §103(a) as being obvious over Antalis et al., WO 98/36054, Samal et al., U.S. Patent 5,278,062, and Egelrud et al., U.S. Patent 5,834,290, all submitted with Applicant's Information Disclosure Statement, in view of Hellgren et al., U.S. Patent 4,801,451, made of record herewith.

Antalis et al. disclose, see Figure 20C, SEQ ID NO:30, pages 10, 18, and Example 15 at pages 52-53 and claims 19-21, 26, and 27, a nucleotide sequence encoding a serine protease designated SP003LA having a deduced amino acid sequence sharing 100% sequence identity with the amino acid sequence of the native T protease from position 26 to position 290, inclusive. The catalytic domain of the SP003LA product that Antalis et al. identify as a serine protease is entirely identical to the catalytic domain of the native protease T disclosed herein, lacking only a portion of the signal peptide region to share complete identity with the protease T amino acid sequence of SEQ ID NO:7 of the instant application and sharing the same activation site sequence, thus the cDNA of SEQ ID NO:30 of Antalis et al. clearly anticipates a nucleic acid molecule encoding a "functional

derivative" of a protease T having the amino acid sequence set forth in SEQ ID NO:7, a derivative protease having a proteolytic activity identical to that of a "protein" present in a non-pharmaceutical composition of claims 25 and 26 herein. Antalis et al. also disclose, pages 38 and 39, expression vectors and host cells comprising a nucleotide sequence encoding a SP003LA serine protease in a context for expression by the host cell, which may be a prokaryotic or eukaryotic host cell. Antalis et al. need not disclose construction of a particular expression vector comprising a SP003LA-encoding nucleotide sequence, or transformation of a particular host cell with such an expression vector, to render the production of a protease present in compositions of claims 25 and 26 herein obvious to one of ordinary skill in the art where a great variety of such vectors and host cells were well-known and commonly-used in the art at the time the invention was made.

Antalis et al. suggest that the SP003LA protease may be used to prepare antisera capable of identifying the protease for diagnosing diseases or medical conditions associated with the absence of, or reduced levels of, the expression of the protease but disclose no process for expressing the SP003LA serine protease in recombinant host cells, nor do they disclose the preparation of non-pharmaceutical compositions comprising the protease. Thus the teachings of Egelrud et al. and Samal et al. are combined with those of Antalis et al. to show that the recombinant production of the serine protease of Antalis et al. would have been obvious to one of ordinary skill in the art and that it would have been obvious to such an artisan to formulate non-pharmaceutical cleaning compositions comprising a recombinantly-produced SP003LA protease having a catalytic activity identical to that of the serine protease T. Egelrud et al. teach, cols. 9-20, and col. 22, lines 25-46, and Figs. 15 and 18, that a polynucleotide, their SEQ ID NO:1, encoding an a newly-discovered and medically-important human serine protease, SCCE, having the amino acid sequence set forth in their SEQ ID NO:2, may be inserted in an expression vector used to transform

eukaryotic host cells and employed in the recombinant expression of the encoded SCCE serine protease, which may be recovered from the transformed cells and then formulated with surfactants, binders, and other compounds to prepare cleaning compositions such as soaps and shampoos. Samal et al. teach, cols. 4-6, the preparation of an expression vector comprising a polynucleotide encoding an eukaryotic serine protease, designated TW7 and having an amino acid sequence set forth in their Fig. 3, the transformation of an eukaryotic host cell with the expression vector, the induction of the recombinant expression of the encoded serine protease TW7 by the transformed host cells, the recovery of the protease from the transformed cells, and then the formulation of the recovered serine protease with surfactants, binders, bleaches, and ancillary compounds to prepare a non-pharmaceutical, detergent, composition useful for laundering fabrics. Hellgren et al. establish that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have prepared a detergent composition comprising an animal serine protease indicated to be medically significant, such as the SCCE protease of Egelrud et al. or the SP003LA protease of Antalis et al., where Hellgren et al. teach, cols. 2-9, that an animal serine protease may be formulated in compositions for topical cleaning of human skin as well as formulated in detergent compositions for laundering fabrics.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce the medically significant human serine protease SP003LA taught by Antalis et al. in order to prepare non-pharmaceutical compositions comprising the protease by inserting a polynucleotide encoding the protease an expression vector in a context for expression, transforming an eukaryotic host cell with the expression vector and inducing the recombinant expression of the encoded protease by the transformed host cells, and then recovering the protease from the transformed cells for formulation in a composition comprising surfactants, binders, bleaches, and other compounds, constituting a detergent

composition useful for laundering fabrics. This is because both Egelrud et al. and Samal et al. teach that eukaryotic serine proteases may be recombinantly expressed by host cells transformed with expression vectors comprising polynucleotides encoding the proteases and that the proteases may be recovered from such cells upon expression for formulation in non-pharmaceutical compositions suitable for cleaning a person or laundry and because Hellgren et al. teach that the serine protease of an animal may be formulated in non-pharmaceutical compositions suitable for cleaning a person as well as formulated in non-pharmaceutical detergent compositions suitable for laundering fabrics.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM-5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. Further fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
July 3, 2003